Research Article
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Evaluation of tear film instability pre and post corneal collagen cross-linking procedure in keratoconus patients

Abstract

Purpose: To evaluate tear film instability in keratoconus patients pre and post CXL procedure.

Study design: Prospective cross-sectional study.

Place and duration of study: Study was conducted at Al Ehsan Welfare eye hospital Lahore from 15th September, 2020 to 15th June, 2021.

Materials and methods: Tear break-up time (TBUT) test was used for determining the stability of the tear film out of 30 patients diagnosed with mild, moderate and severe keratoconus and tear film stability was assessed before and after CXL procedure by measuring tear break up time. Data was collected by using non-probability convenient sampling method. The patients were excluded if they had any previous dry eye syndrome, tear film instability, refractive surgery, other ocular surface abnormalities, cataract surgery and contact lens use before the CXL procedure. Pre and post-operative tear break up time was measured by performing TUBT test. Patients were selected between the age 25 to 35 years. In TBUT, sodium fluorescein dye was used and the tear film was observed with slit lamp under low magnification while the patient was instructed to avoid blinking while time was calculated until first dry spot appearance. SPSS version 21 was used for data analysis and Mcneemar's test (kappa statistics) was applied with significance of $p < 0.05$.

Results: Results shows that pre CXL tear breakup time of 22 patients was normal (10-15) sec while 8 patients were observed with borderline tear break up time less than 10 sec with percentage of 73.3% and 26.7 % respectively. Results of Post TBUT after one week of CXL procedure shows variation in values of tear break up time which shows decrease of tear break up time less than 10 sec of 12 patients and 18 patients with significantly reduced tear break up time less than 5 sec was recorded with percentage of 40.% and 60. % respectively. After two weeks of procedure it was recorded that tear break up time of 4 patients was normal (10-15 sec) post tear break up time, while tear break up time of 18 patients was noted borderline (<10 sec) and 8 patient with reduced post tear break up time (<5sec) with percentage of 13.3 % , 60 % and 26.7% respectively. After one month of CXL the tear break up time was significantly improved as compared to one and two weeks of postoperative procedure of CXL as the corneal epithelium was regenerated.

Conclusion: This study concludes that tear breakup time was significantly reduced after CXL procedure. TBUT was normal before the CXL but after CXL due to destruction of corneal epithelium the TBUT was reduced. Thus results reveals instability of tear films occurs after CXL procedure.

Keywords: CXL, TBUT, keratoconus, corneal epithelium, fluorescein strips

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Introduction

Keratoconus is the ectatic type of bulging of cornea. It normally happens after 20s in both gender despite of any cause. Early stages are normally detected after corneal topography. Corneal bulge will cause high nearsightedness and against the rule astigmatism. The management of this diseases is done according to the severity of disease. The patients with mild Keratoconus are treated through glasses as the disease progresses the treatment changes. The mild and moderate cases are treated with contact lenses or CXL and more serious cases are treated with keratoplasty.[1]

Keratoconus is may be caused by reduced bio-mechanical strength of corneal tissue which will then affect the vision of a patient. The difference in keratoconus corneas and normal corneas in bio-mechanical constants are shown experimentally, but the effect of morphological or biochemical cause is unknown. By using various techniques may increase the tensile strength of polymers and collagenous tissue.[2]

Corneal cross linking is an intrusive technique that utilizes ultraviolet and eye drops to reinforce the collagen filaments in the cornea. The strategy is utilized for patients with keratoconus, a condition wherein the cornea becomes slender and frail. The essential objective of CXL is to halt the continuation of corneal dilatation. To improve quality of corneal tissue, the riboflavin is combined with bright A light (UVA).[3]

Corneal cross linkage is an outpatient technique that regularly goes on for about 60 minutes. While the treatment won't correct vision

or dispense with the requirement for glasses as well as contact focal points, it can help keep up the current degree of vision and is intended to keep vision from deteriorating. It can likewise encourage the utilization of contact focal points. CXL is a healthy and effective way to slow down the degradation of keartoconus while improving visual control.[4] Dry eye is a multifactorial disorder of the tears and visual surface that consequences in signs of irritation, visual defects, and tear film instability with function harm to the visual surface of eye. It followed with the aid of extended concentration of the tear film and infection of the visual surface. Dry eye is most common disorder of ocular surface which usually occurs when instability of ocular surface occurs due to disruption of corneal epithelium resulting in decreased tear break up time. Reduced tear break up time shows unstable ocular surface presenting symptoms of discomfort, irritation, watering and photophobia.[5]

There is limited evidence regarding tear function after CXL in keratoconus. This study aims to investigate CXL effect on tear film in keratoconus patients after CXL. Therefore, we evaluated the tear function in patients with keratoconus before CXL and one week, two weeks and one months after the procedure.

Methodology

A prospective cross-sectional study was conducted in the time span of six months. The participants of study were selected through non-probability convenient sampling method. Sample size was consist of 30 patients. The age of the patients ranges from 25 to 35 years. The patients who diagnosed with mild, moderate and severe keratoconus were included for collagen cross linkage (CXL) procedure were selected for the study. The patients were excluded from the study who had other ectactic conditions, other ocular surface abnormalities, diabetes, dry eye syndrome, tear film instability and pellucid marginal degeneration. Both genders were included in the study. The TBUT (tear break-up time test) was used before and after the procedure of CXL through slit lamp under low magnification. First a fluorescein was instilled into the eye of patients through the fluorescein strip and patient was asked to blink few time to spread tears evenly on ocular surface and then on slit lamp they were asked to stop blinking on slit lamp then time was noted through the stopwatch between the last blink and first break appears on the surface of tear film.

The readings were taken before the CXL procedure and after one week ,two weeks and one month of the CXL procedure. Questionnaire was designed to collect data for study.

Results

Overall 30 patients were selected in this study. There were 19 patients of 25-29 years and 11 patients of 30-35 years of age. On basis of gender distribution there were 21 female and 9 male patients in study. Further type of keratoconus was also checked according to the curvature of cornea and divided into the three categories mild, moderate and severe.

The cross-tabulation between the pre-TBUT and post-TBUT of one week ,two weeks and one month is shown in the Table 1. The TBUT was divided into three categories normal (>10 sec), borderline (<10 sec) and reduce (<5 sec).The patients with reduce tear break up time (<5 sec) were considered as patients with instable tear film. According to the Table 1 in pre TBUT 22 patients found normal and 8 patients were in borderline category After one week of CXL, the TBUT reduces as the 12 patients tear break up time was at borderline and 8 found reduce less then 5 seconds which was due to the removal of corneal epithelium during the procedure of CXL which would cause the tear film instability in patients. After two week of CXL ,TBUT was again assessed in the patients the results was significantly improved then the first week as just 8 patients had reduce tear break up time (<5 sec) because the corneal epithelium regenerate in 7-10 days. Tear break up time assessed after one month of CXL procedure the just 2 patients had reduced (<5secs) TBUT. A comparison chart is given to show the reduction of TBUT after the CXL procedure and significantly improvement as the corneal epithelium regenerates in Figure 1.

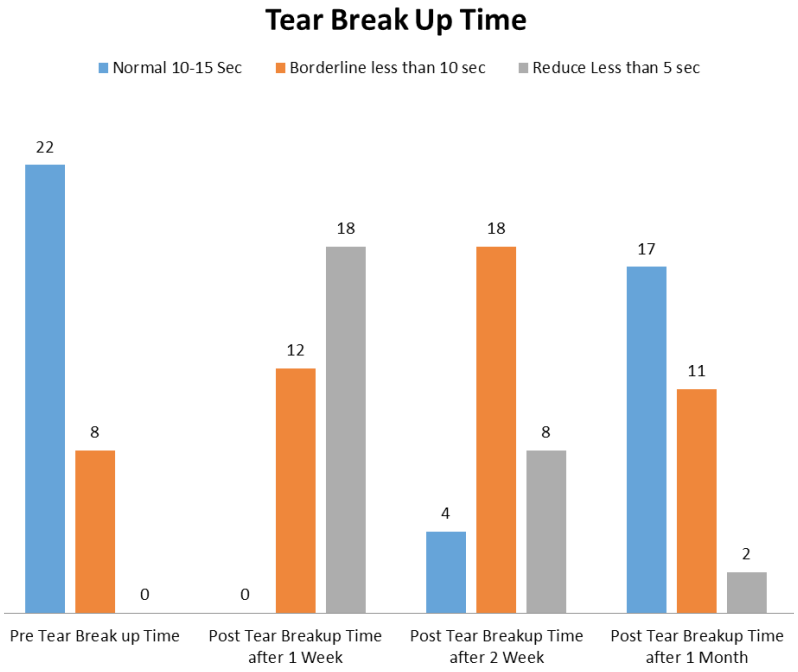

Figure 1 Comparison chart between pre TBUT and post TBUT of one week, two week and one month.

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On division of keratoconus types, seven patient (23.3%) were presented with mild keratoconus. Fourteen patients (with highest ratio) (46.7%) enrolled for this study were with moderate keratoconus. Nine patients (30%) were presented with sever kind of keratoconus. As the comparison shows in bar chart shows tear breakup time was significantly reduced after CXL, the patient's TBUT was normal before the CXL after CXL due to destruction corneal epithelium the TBUT was reduced significantly after one week. But tear break up time was significantly improved after two weeks and one month as corneal epithelium regenerates.

Table 1 Cross-tabulation of pre TBUT and post TBUT of one week, two weeks and one month of CXL procedure

	Normal(>10sec)	Borderline (<10)	Reduce (<5)	Total number of patient
Pre TBUT	22	8	0	30
Post TBUT 1st week	0	12	18	30
Post TBUT 2nd week	4	18	8	30
Post TBUT one month	17	11	2	30

Table 2 Frequency distribution according to age

		Frequency	Percent
Age-wise	age between 25-29 years	19	63.3
	age between 30-35 years	11	36.7
	Total	30	100

For this study 30 patients were enrolled. 19 patients out 30 were between the age of 25 to 29 (63.3). And 11 patients which enrolled were age between 30 to 35 (36.7)

Table 3 Frequency distribution according to gender

		Frequency	Percent
Gender	female	21	70
	male	9	30
	Total	30	100

21 out of 30 enrolled patients were female (70%) and 9 patient were male (30%) (2:1)

Table 4 Frequency distribution according to stages of keratoconus

		Frequency	Percent
Keratoconus stage	Mild	7	23.3
	moderate	14	46.7
	Severe	9	30
	Total	30	100

Discussion

The study was conducted by turkey in 2020, they investigate the long-term effects that corneal collagen cross linking procedure has effect on the ocular surface and tear function in keratoconus. They concluded that the improvement in Tear break up time, conjunctival squamous metaplasia, and goblet cell density shows a good impact of corneal collagen cross linkage procedure on the visual surface and tear film in keratoconus, probably because of the decreased corneal inconsistency after corneal collagen cross linkage procedure.[6] In our study we explained that, any ocular surgery cause the destruction of goblet cell density which regulate the function of mucin layer. The reduction in density of goblet cell cause the tear film instability.

The study was conducted in South Korea in 2013, they investigate tear function, ocular surface changes, and corneal sensitivity in patients with asymmetrical keratoconus (KC). They concluded that mean corneal affect-ability and Schirmer test esteems were altogether lower in the Keratoconus and subclinical Keratoconus eyes contrasted with the control eyes. The conjunctiva of Keratoconus and subclinical Keratoconus eyes showed essentially higher evaluations of squamous metaplasia and goblet cell misfortune contrasted and the benchmark group. In any case, no critical difference in tear osmolarity was found among the groups. The corneal affect-ability and visual surface changes were critical in the subclinical Keratoconus and Keratoconus eyes contrasted and the control subjects. Visual surface disorders in Keratoconus was portrayed by tear inadequacy disease and strange impression cytology results. Nonetheless, no critical distinction in tear osmolarity was found among the sets of patients. The lessening in corneal affect-ability and visual surface change might be related with the pathogenesis of visual surface changes in Keratoconus and the movement of the disorder.[7] In contrast of this study we also explained that the keratoconus patient is treated by corneal collagen cross linking procedure which cause the ocular surface damage like epithelium destruction. And due to epithelium destruction and reduction in goblet cell density the marked tear film instability is occurred.

The study was conducted in turkey in 2017, to investigate the alterations in the ocular surface and tear film parameters 3 months after accelerated corneal collagen cross-linking (A-CXL) in progressive keratoconus (KC) patients. They concluded that just metaplastic changes and a decrease in the thickness of the goblet cells were seen in conjunctival IC, which is most likely on account of the harmfulness of ultraviolet-A three months after A-corneal collagen cross linkage procedure. In any case, these outcomes do not prompt disintegration in tear break up time. In this examination, A-corneal collagen cross linkage procedure has no harmful impact on visual surface and tear function, which are significant for visual quality.[8] In our study we also explained the association of CXL procedure and ocular surface damage. The CXL procedure cause the tear film instability due to epithelium destruction. But after the one month the TBUT is significantly improved and eye is regulate on normal function but some cases showed that reduction in goblet cell density cause the some distortion in TBUT.

The study was conducted in Italy in 2008, they investigate to early and late micro morphological modifications of cross-linked corneas in vivo by means of Heidelberg Retinal Tomography (HRT) II confocal microscopy. They concluded that no harm to the limbal area was noticed. Epithelial regrowth was finished following 4 days of delicate contact focal point guaze. The life systems of the sub epithelial plexus was reestablished one year after the activity with full corneal affect-ability. Expanded thickness of extracellular network in late post-

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operative period showed cross-linked collagen to a profundity of three hundred and 40µm communicated by a late outline. In vivo confocal microscopy showed early and late alteration of corneal microstructure after the treatment. The 3year soundness of corneal collagen cross linkage procedure recorded could be identified with expanded cross-joins arrangement, union of all-around organized collagen and new lamellar interconnections.[9] In contrast with this study explained that the CXL procedure done with the removal of epithelium layer. Due to destruction of epithelium layer the tear film instability is occurred. After 7-10 days the epithelium is regenerated and TBUT time is significantly improved. But in some cases due to reduction in goblet cell density the tear film instability lasts for 1-3 month.

The study was conducted in Spain in 2017, Based on the relationship between keratoconus and dry eye, the aim of this study was to evaluate changes in signs and symptoms of dry eye in keratoconus patients before and after intrastromal corneal ring surgery. They concluded that intrastromal corneal ring a medical procedure initiates changes improving dry eye indications however no progressions were found in indications of dry eye after a medical procedure in keratoconus patients aside from the MCH that increments radically. More investigations are expected to explain the explanation of its improvement.[10] In our study we explained the association between the keratoconic eyes, CXL procedure and dry eye. The CXL procedure is done on the keratoconic eye which markedly having the effect on ocular surface especially on tear film (due to epithelium degeneration) which cause dry eye.

Our study fairly highlighted that the tear film instability after corneal cross linking procedure in keratoconus patients. In keratoconus patient we treat the keratconic eye by corneal cross linking procedure. After this procedure we seen that some dry eye issues is occur. Dry eye has emerged as one of the most important post- operative complication after the refractive surgeries because in the most of the surgeries we use the cornea as well corneal epithelium. In the refractive surgeries the corneal epithelium is damaged and directly they cause the tear film instability which leads to dry eye.in the procedure of the corneal cross linking procedure, the corneal epithelium is damaged and dry eye occurs. After the CXL the corneal epithelium is regenerated in a week. However, we seen that tear layer is disturbed with the degeneration of corneal epithelium. Dry eye syndrome is peak at the first week and most probably till after 1 month. This study was helpful for the community by examining the tear film stability pre operatively and post operatively post-operative the tear stability was less after passing some time in some patients the teat film was recovered but not in all patients so they need a proper care regarding their tear film. Generally dry eye was ignored post operatively the patients would suffer from the symptoms of dry eye so before they suffer from any discomfort the lubricants and artificial tears were recommended to them. More over further studies was explained the different refractive surgeries and related the dry eye syndrome with surgeries.

It is recommended that Guide the patient about Dry eye complication after the CXL procedure. After the CXL procedure, prescribe the artificial tear and lubricants to treat the dry eye. The dry eye also cause disturbance in vision, so counsel the patient about that, with the passage of time as the vision is getting normal.

Conclusion

This study concludes that tear breakup time was significantly reduced after CXL procedure. Tear break up time was normal before the CXL but after CXL procedure it was decreased due to destruction of corneal epithelium. Thus results reveals instability of tear films occurs after CXL procedure there was found statistically difference in pre and post tear break up time values. But tear break up time was significantly improved after two weeks and one month of CXL procedure respectively as shown in results as corneal epithelium regenerates. So, that pathogenic factors causing tear film instability after CXL tends to be corneal epithelium and microscopic ocular surface damage throughout CXL procedure.

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Conflicts of interest

There are no financial conflicts of interest.

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